

AMENDMENTS TO THE CLAIMS:

1. (original) An isolated OPAL1 polynucleotide comprising a nucleotide sequence selected from the group consisting of:
  - (a) SEQ ID NO:1 or 3;
  - (b) a complement of SEQ ID NO:1 or 3;
  - (c) a subunit of SEQ ID NO:1 or 3 consisting of at least 60 contiguous nucleotides;
  - (d) a nucleotide sequence that hybridizes to SEQ ID NO:1 or 3;
  - (e) a nucleotide sequence having at least 95% identity to SEQ ID NO:1 or 3
  - (f) a nucleotide sequence having at least 98% identity to SEQ ID NO:1 or 3
  - (g) a nucleotide sequence encoding a polypeptide encoded by SEQ ID NO:2 or 4.
2. (original) An isolated OPAL1 polynucleotide comprising the nucleotide sequence SEQ ID NO:1 or 3.
3. (original) An isolated OPAL1 polynucleotide comprising a nucleotide sequence encoding the amino sequence SEQ ID NO:2 or 4.
4. (original) An isolated OPAL1 polypeptide comprising an amino acid sequence selected from the group consisting of:
  - (a) SEQ ID NO:2 or 4;
  - (b) a subunit of SEQ ID NOs:2 or 4 having at least 20 contiguous amino acids;
  - (c) an amino acid sequence having at least 90% identity to SEQ ID NOs:2 or 4
  - (c) an amino acid sequence having at least 95% identity to SEQ ID NOs:2 or 4.
5. (original) An isolated OPAL1 polypeptide comprising the amino acid sequence SEQ ID NO:2 or 4.

6. (original) An isolated OPAL1 polypeptide comprising an amino acid sequence having at least about 90% identity to SEQ ID NO:2 or 4, wherein the polypeptide retains at least a portion of the biological activity of SEQ ID NO:2 or 4.

7. (original) An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

8. (Currently amended) A host cell transformed or transfected with an expression vector according to claim 3 7.

9. (Original) An isolated antibody, or antigen-binding fragment thereof, that specifically binds to the polypeptide of claim 4.

10. (Currently amended) A method for predicting therapeutic outcome in a leukemia patient comprising:

- (a) obtaining a biological sample from a patient;
- (b) determining the expression level for an OPAL1 gene product to yield an observed OPAL1 gene expression level; and
- (c) comparing the observed OPAL1 gene expression level for the OPAL1 gene product to a control OPAL1 gene expression level selected from the group consisting of:
  - (i) the OPAL1 gene expression level for the OPAL1 gene product observed in a control sample; and
  - (ii) a predetermined OPAL1 gene expression level for the OPAL1 gene product;

wherein an observed OPAL1 expression level that is higher than the control OPAL1 gene expression level is indicative of predicted remission or an observed OPAL 1 expression level that is lower than the control OPAL1 gene expression level is indicative of a potential need for a more aggressive therapeutic intervention.

11. (Currently amended) The method of claim 10 further comprising determining the expression level for a G1 or G2 gene product to yield an observed G1 or G2 gene expression level; and comparing the observed G1 or G2 gene expression level for the G1 or G2 gene product to a control G1 or G2 gene expression level selected from the group consisting of: (i) the G1 or G2 gene expression level for the G1 or G2 gene product observed in a control sample; and (ii) a predetermined G1 or G2 gene expression level for the G1 or G2 gene product; wherein an observed G1 or G2 expression level that is different from the control G1 or G2 gene expression level is further indicative of predicted remission or the potential need for a more aggressive therapeutic intervention.

12. (original) A method for detecting an OPAL1 polynucleotide in a biological sample comprising:

- (a) contacting the sample with the polynucleotide of claim 1 under conditions in which the polynucleotide selectively hybridizes to an OPAL1 gene; and
- (b) detecting hybridization of the nucleic acid molecule to the OPAL1 gene in the sample.

13. (original) A method for detecting an OPAL1 protein in a biological sample comprising:

- (a) contacting the sample with the antibody according to claim 9 under conditions in which the antibody selectively binds to an OPAL1 protein; and
- (b) detecting the binding of the antibody to the OPAL1 protein in the sample.

14. (original) A pharmaceutical composition comprising:

- (a) a therapeutic agent selected from the group consisting of:
  - (i) a polynucleotide of claim 1;
  - (ii) a polypeptide of claim 4; and
  - (iii) a compound that enhances the activity of the polypeptide of claim 4;and
- (b) a pharmaceutically acceptable carrier.

15. (original) The pharmaceutical composition of claim 14 further comprising:

- (a) a second therapeutic agent selected from the group consisting of:
  - (i) a polynucleotide encoding G1 or G2;
  - (ii) a G1 or G2 polypeptide; and
  - (iii) a compound that alters the activity of a G1 or G2 polypeptide.

16. (original) A method for treating leukemia comprising administering to a leukemia patient a therapeutic agent that increases the amount or activity of the polypeptide of claim 4 in the patient.

17. (original) The method of claim 16 further comprising administering to a leukemia patient a therapeutic agent that alters the amount or activity of a G1 or G2 polypeptide.

18. (original) A method for screening compounds useful for treating leukemia comprising:

- (a) determining the expression level for an OPAL1 gene product in a cell culture to yield an observed OPAL1 gene expression level prior to contact with a candidate compound;
- (b) contacting the cell culture with a candidate compound;
- (c) determining the expression level for the OPAL1 gene product in the cell culture to yield an observed OPAL1 gene expression level after contact with the candidate compound; and
- (d) comparing the observed OPAL1 gene expression level before and after contact with the candidate compound wherein an increase in OPAL1 gene expression level after contact with the compound is indicative of therapeutic utility.

19. (original) A method for screening compounds useful for treating leukemia comprising:

- (a) contacting an experimental cell culture with a candidate compound;
- (b) determining the expression level for an OPAL1 gene product in the cell culture to yield an experimental OPAL1 gene expression level; and

(b) comparing the experimental OPAL1 expression level to the expression level of the OPAL1 gene product in a control cell culture, wherein a relative difference in the gene expression levels between the experimental and control cultures is indicative of therapeutic utility.

20. (original) A method for evaluating a compound for use in treating leukemia, comprising:

- (a) obtaining a first biological sample from a patient;
- (b) determining the expression level for an OPAL1 gene product in the first biological sample to yield an observed OPAL1 gene expression level prior to administration of a candidate compound;
- (c) administering a candidate compound to the patient;
- (d) obtaining a second biological sample from the patient;
- (e) determining the expression level for an OPAL1 gene product in the second biological sample to yield an observed OPAL gene expression level after administration of the candidate compound; and
- (f) comparing the observed OPAL1 gene expression levels before and after administration of the candidate compound to determine whether the compound has therapeutic utility.

21. (original) A method for classifying leukemia in a patient comprising:

- (a) obtaining a biological sample from a patient;
- (b) determining the expression level for a selected gene product to yield an observed gene expression level; and
- (c) comparing the observed gene expression level for the selected gene product to a control gene expression level selected from the group consisting of:
  - (i) the expression level observed for the gene product in a control sample;and
  - (ii) a predetermined expression level for the gene product;wherein an observed expression level that differs from the control gene expression level is indicative of a disease classification.

22. (original) The method of claim 21 wherein the disease classification comprises predicted remission or therapeutic failure.
23. (currently amended) The method of claim 22 wherein the gene product is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.
24. (original) The method of claim 21 wherein the disease classification comprises a classification based on karyotype.
25. (original) The method of claim 21 wherein the disease classification comprises leukemia subtype.
26. (original) The method of claim 21 wherein the disease classification comprises a classification based on disease etiology.
27. (original) A method for classifying leukemia in a patient comprising:
- (a) obtaining a biological sample from a patient;
  - (b) determining a gene expression profile for selected gene products to yield an observed gene expression profile; and
  - (c) comparing the observed gene expression profile for the selected gene products to a control gene expression profile for the selected gene products that correlates with a disease classification;
- wherein a similarity between the observed gene expression profile and the control gene expression profile is indicative of the disease classification.
28. (original) The method of claim 27 wherein the disease classification comprises predicted remission or therapeutic failure.

29. (Currently amended) The method of claim 28 wherein at least one of the gene products is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

30. (original) The method of claim 27 wherein the disease classification comprises a classification based on karyotype.

31. (original) The method of claim 27 wherein the disease classification comprises leukemia subtype.

32. (original) The method of claim 27 wherein the disease classification comprises a classification based on disease etiology.

33.(original) A method for screening compounds useful for treating acute leukemia comprising:

(a) determining the expression level for a selected gene product in a cell culture to yield an observed expression level for the gene product prior to contact with a candidate compound, wherein the selected gene product is correlated with therapeutic outcome;

(b) contacting the cell culture with a candidate compound;

(c) determining the expression level for the selected gene product in a cell culture to yield an observed gene expression level after contact with the candidate compound;  
and

(d) comparing the observed expression levels of the selected gene product before and after contact with the candidate compound wherein a modulation of gene expression level after contact with the compound is indicative of therapeutic utility.

34. (Currently amended) The method of claim 33 wherein the gene product is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

35. (original) A method for screening compounds useful for treating acute leukemia comprising:

- (a) determining a gene expression profile for selected gene products in a cell culture to yield an observed gene expression profile prior to contact with a candidate compound, wherein the selected gene products are correlated with therapeutic outcome;
- (b) contacting the cell culture with a candidate compound;
- (c) determining a gene expression profile for the selected gene products in the cell culture to yield an observed gene expression profile after contact with the candidate compound; and
- (d) comparing the observed expression profiles before and after contact with the candidate compound to determine whether the compound has therapeutic utility.

36. (Currently amended) The method of claim 35 wherein at least one of the gene products is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

37. (original) A method for screening compounds useful for acute treating leukemia comprising:

- (a) contacting an experimental cell culture with a candidate compound;
- (b) determining the expression level for a selected gene product in the cell culture to yield an experimental gene expression level for the gene product, wherein the selected gene product is correlated with therapeutic outcome; and
- (c) comparing the experimental gene expression level to the expression level of the selected gene product in a control cell culture, wherein a relative difference in the gene expression levels between the experimental and control cultures is indicative of therapeutic utility.

38. (Currently amended) The method of claim 37 wherein the gene product is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein,



PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

39. (original) A method for screening compounds useful for acute treating leukemia comprising:

- (a) contacting an experimental cell culture with a candidate compound;
- (b) determining a gene expression profile for selected gene products in the cell culture to yield an experimental gene expression profile, wherein the selected gene products are correlated with therapeutic outcome; and
- (c) comparing the experimental gene expression profile to the gene expression profile for the selected gene products in a control cell culture to determine whether the compound has therapeutic utility.

40. (Currently amended) The method of claim 39 wherein at least one of the gene products is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

41. (original) A method for evaluating a compound for use in treating leukemia, comprising:

- (a) obtaining a first biological sample from a patient;
- (b) determining a gene expression profile for selected gene products in the first biological sample to yield an observed gene expression profile prior to administration of a candidate compound, wherein the selected gene products are correlated with therapeutic outcome;
- (c) administering a candidate compound to the patient;
- (d) obtaining a second biological sample from the patient;
- (e) determining a gene expression profile for the selected gene products in the second biological sample to yield an observed gene expression profile after administration of the candidate compound; and

(f) comparing the observed gene expression profiles before and after administration of the candidate compound to determine whether the compound has therapeutic utility.

42. (Currently amended) The method of claim 41 wherein at least one of the gene products is produced by a gene selected from the group consisting of OPAL1, G1, G2, FYN binding protein, PBK1, osteonectin and any of the genes listed in ~~Table 42~~ Tables 4-12, 15-18; 20, 24, 29-42, 47 and 53-57.

43. (new) An isolated antibody, or antigen-binding fragment thereof, that specifically binds to the polypeptide of claim 5.

44. (new) The method of claim 24 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 13, 14, 21, 26 or 27 or Figs. 8, 14, 16, 17 or 18.

45. (new) The method of claim 24 wherein the leukemia subtype is ALL or AML.

46. (new) The method of claim 45 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 51 or 52.

47. (new) The method of claim 24 wherein the leukemia subtype is T lineage ALL or B lineage ALL.

48. (new) The method of claim 47 wherein the gene product is produced by a gene selected from any of the genes listed in Fig. 7.

49. (new) The method of claim 26 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 43, 45, 58-60 or Fig. 15.

50. (new) The method of claim 26 wherein the leukemia is a pediatric ALL and wherein the gene product is produced by a gene listed in Table 43.

51. (new) The method of claim 26 wherein the leukemia is an infant leukemia and wherein the gene product is produced by a gene selected from any of the genes listed in Tables 45, 58-60 or Fig. 15.

52. (new) The method of claim 30 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 13, 14, 21, 26 or 27 or Figs. 8, 14, 16, 17 or 18.

53. (new) The method of claim 31 wherein the leukemia subtype is ALL or AML.

54. (new) The method of claim 53 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 51 or 52.

55. (new) The method of claim 31 wherein the leukemia subtype is T lineage ALL or B lineage ALL.

56. (new) The method of claim 55 wherein the gene product is produced by a gene selected from any of the genes listed in Fig. 7.

57. (new) The method of claim 32 wherein the gene product is produced by a gene selected from any of the genes listed in Tables 43, 45, 58-60 or Fig. 15.

58. (new) The method of claim 32 wherein the leukemia is a pediatric ALL and wherein the gene product is produced by a gene listed in Table 43.

59. (new) The method of claim 32 wherein the leukemia is an infant leukemia and wherein the gene product is produced by a gene selected from any of the genes listed in Tables 45, 58-60 or Fig. 15.

60. (New) The method of claim 10 wherein an observed OPAL 1 expression level that is higher than the control OPAL1 gene expression level is indicative of predicted remission.

61. (New) The method of claim 10 wherein an observed OPAL1 expression level that is lower than the control OPAL1 gene expression level is indicative of the potential need for a more aggressive therapeutic intervention.

62. (New) The method of claim 11 wherein an observed OPAL 1 expression level that is lower than the control OPAL1 expression level and an observed G1 gene expression level that is lower than the control G1 gene expression level is indicative of the potential need for a more aggressive therapeutic intervention.

63. (New) The method of claim 11 wherein an observed OPAL 1 expression level that is lower than the control OPAL1 expression level, an observed G1 gene expression level that is higher than the control G1 gene expression level and an observed G2 gene expression level that is higher than the control G2 gene expression level is indicative of the potential need for a more aggressive therapeutic intervention.

64. (New) The method of claim 11 wherein an observed OPAL 1 expression level that is higher than the control OPAL1 expression level and an observed G1 gene expression level that is lower than the control G1 gene expression level is indicative of predicted remission.

65. (New) The method of claim 11 wherein an observed OPAL 1 expression level that is higher than the control OPAL1 expression level, an observed G1 gene expression level that is higher than the control G1 gene expression level and an observed G2 gene expression level that is higher than the control G2 gene expression level is indicative of predicted remission.

66. (New) The method according to claim 18 comprising the additional steps of determining in step (a) the expression level for a G1 gene product in said cell culture to yield an observed G1 gene expression level, determining in step (c) the expression level for the G1 gene product in the cell culture to yield an observed G1 gene expression level after contact with the candidate compound, and comparing in step (d) the observed G1 gene expression level before and after contact with the candidate compound wherein an increase in OPAL1 gene expression level after contact with the candidate compound combined with a decrease in G1 gene expression level after contact with the candidate compound is indicative of therapeutic utility.

67. (New) The method according to claim 18 comprising the additional steps of determining in step (a) the expression level for a G1 gene product in said cell culture to yield an observed G1 gene expression level, determining in step (c) the expression level for the G1 gene product in the cell culture to yield an observed G1 gene expression level after contact with the candidate compound, and comparing in step (d) the observed G1 gene expression level before and after contact with the candidate compound wherein an increase in OPAL1 gene expression level after contact with the candidate compound combined with a decrease in the G1 gene expression level after contact with the candidate compound is indicative of therapeutic utility.

68. (New) The method according to claim 18 comprising the additional steps of determining in step (a) the expression level for a G1 gene product and a G2 gene product in said cell culture to yield an observed G1 gene expression and an observed G2 gene expression, determining in step (c) the expression level for the G1 and G2 gene products in the cell culture to yield observed G1 and G2 gene expression levels after contact with the candidate compound, and comparing in step (d) the observed G1 and G2 gene expression levels before and after contact with the candidate compound wherein an increase in OPAL1 gene expression level after contact with the candidate compound combined with an increase in the G1 and G2 gene expression levels after contact with the candidate compound is indicative of therapeutic utility.

69. (New) The method according to claim 20 comprising the additional steps of determining in step (b) the expression level for a G1 gene product in said first biological sample to yield an observed G1 gene expression, determining in step (e) the expression level for the G1 gene product in the second biological sample to yield an observed G1 gene expression level, and comparing in step (f) the observed G1 gene expression level before and after administering the candidate compound wherein an increase in OPAL1 gene expression level after administering the candidate compound combined with a decrease in G1 gene expression level after administering the candidate compound is indicative of therapeutic utility.

70. (New) The method according to claim 20 comprising the additional steps of determining in step (b) the expression level for a G1 gene product in said first biological sample to yield an observed G1 gene expression level, determining in step (e) the expression level for the G1 gene product in the second biological sample to yield an observed G1 gene expression level, and comparing in step (f) the observed G1 gene expression level before and after administering the candidate compound wherein an increase in OPAL1 gene expression level after administering the candidate compound combined with a decrease in the G1 gene expression level after administering the candidate compound is indicative of therapeutic utility.

71. (New) The method according to claim 18 comprising the additional steps of determining in step (b) the expression level for a G1 gene product and a G2 gene product in said first biological sample to yield an observed G1 gene expression and an observed G2 gene expression, determining in step (d) the expression level for the G1 and G2 gene products in the second biological sample cell culture to yield observed G1 and G2 gene expression levels, and comparing in step (f) the observed G1 and G2 gene expression levels before and after administering the candidate compound wherein an increase in OPAL1 gene expression level after contact with the candidate compound combined with an increase in the G1 and G2 gene expression levels after contact with the candidate compound is indicative of therapeutic utility.

72. (New) The method according to any of claims 20 and 69-71 wherein said leukemia is acute lymphoblastic leukemia (ALL).

73. (New) The method according to any of claims 20, 69-71 wherein said leukemia is acute myeloid leukemia (AML).

74. (New) The method of claim 33 wherein the gene product is produced by the OPAL1 gene and at least one additional gene selected from the group consisting of G1 or G1 and G2.

75. (New) The method of claim 35 wherein the gene product is produced by the OPAL1 gene and at least one additional gene selected from the group consisting of G1 or G1 and G2.

76. (New) The method of claim 37 wherein the gene product is produced by the OPAL1 gene and at least one additional gene selected from the group consisting of G1 or G1 and G2.

77. (New) The method of claim 39 wherein the gene products are produced by the OPAL1 gene and at least one additional gene selected from the group consisting of G1 or G1 and G2.

78. (New) The method of claim 41 wherein the gene products are produced by the OPAL1 gene and at least one additional gene selected from the group consisting of G1 or G1 and G2.